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| EXAMINER | |
|---|---|
| PORTNER, VIRGINIA ALLEN | |
| **ART UNIT** | **PAPER NUMBER** |
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Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/488,737 | LISSOLO, LING | |
| | Examiner | Art Unit | |
| | Ginny Portner | 1645 | |

*-- The MAILING DATE of this communicati n appears on the cover sheet with the correspondence address --*

**Period f r Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☐ Responsive to communication(s) filed on *29 August 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☐ Claim(s) *1,3-7,10,11,14-29 and 31-41* is/are pending in the application.

4a) Of the above claim(s) *21,25-27,31 and 32* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *1,3,5-7,10,11,14-20,22-24,28,29 and 33-41* is/are rejected.

7)☐ Claim(s) *4* is/are objected to.

8)☒ Claim(s) *1,3-7,10,11,14-29 and 31-41* are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Claims 1, 3-7, 10-11, 14-29, 31-41 are pending.

Claims 2, 8-9, 12-13 and 30 have been canceled.

Claims 21, 25-27, 31-32 stand withdrawn from consideration.

Claims 1, 3-7, 10-11, 14-20, 22-24, 28-29, 33-41 are under consideration.

1. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

***Continued Examination Under 37 CFR 1.114***

2. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on August 29, 2003 has been entered.

***Allowable Subject Matter***

3. Claim 4 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. A claim directed to --An isolated and purified Helicobacter pylori protein of the order of 50 kDa, wherein the N-terminal amino acid sequence is SEQ ID No. 1--- would define over the prior art of record.

**Objections/Rejections Withdrawn**

4. Claims 14-15 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, in light of the amendment of the claims to recite active move method steps.

5. Claim 16, 19, 29 and 30 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, in light of the amendment of the claims to clearly set forth the invention, and the cancellation of claim 30.

6. Claim 17 rejected under 35 U.S.C. 101 has been obviated in light of the amendment of claim 17 to recite an isolated product.

**Rejections Maintained**

7. Claims 1,3,5-7,19,22-24,28-29,33,35,38,41 are rejected under 35 U.S.C. 102(b) as being anticipated by **Husson et al** (1993), for reasons of record in papers 15 and 19.

8. Claims 1, 3, 5-7, 10-11 and 14-19, 22-24, 28-29 and 33-41 are rejected under 35 U.S.C. 102(e) as being anticipated by **Calenoff** (US Pat.5,567,594, filing date: December 20, 1993), as previously applied to claims 1-9 and 15, for reasons of record in papers 15 and 19.

9. Claims 7,19-20 and 41 are rejected under 35 U.S.C. 102(b) as being anticipated by **Ferrero et al** (1995),for reasons of record in papers 15 and 19.

10. Claims 7, 10-11, 14-15, 41 are rejected under 35 U.S.C. 102(b),as being anticipated by **Bolin et al** (1995),for reasons of record in papers 15 and 19.

11. Claims 1,3, 5-7,10-11 and 14-15,19, 22-24, 28-29, 33, 35, 38, 41 are rejected under 35 U.S.C. 102(b) as being anticipated by **Doig et al** (1994), for reasons of record.

12. Claims 1,5-6, 7,10-11,15, 19, 23-24, 28,33,35 and 41 are rejected under 35 U.S.C. 102(b) as being anticipated by **Alemohammad** (US Pat.5,262,156), for reasons of record.

13. Claims 7, 19-20, 28-29 and 41 are rejected under 35 U.S.C. 102(e) as being anticipated by **Pronovost et al** (US Pat. 5,814,455 and 5,846,751), for reasons of record.

14. Claims 1 (page 10, Table 1, saline or incomplete Freunds, urease has two protein portions UreA and UreB, one being about 30 kDa and the other about 60 kDa), 5-7, 10-11, 14,17-18, 19-20,23-24, 28, 33,35-36, 41 are rejected under 35 U.S.C. 102(b) as being anticipated by **Ruiz et al** (WO94/06474), for reasons of record.

***Response to Arguments***

**Please Note**: It is the position of the examiner that composition claims which recite the phrase "consisting essentially of" may have additional components added to the composition as long as the basic and novel characteristic of the composition is maintained. The phrase "consisting essentially of" is being read as open language as what characteristic of the composition must

not be altered has not been defined. At page 3 of the instant specification, lines 6-10, the definition of the phrase "substantially purified form" is set forth to be mean "the protein is separated from the medium in which it exists naturally. It is the position of the examiner that this definition reads on a whole cell lysate, and the claimed invention is directed to a membrane fraction of this composition, which would define a composition that would contain a plurality of Helicobacter pylori membrane proteins; additional embodiments read on fractioned H.pylori membrane proteins, and antibodies directed to the proteins and fragments of the proteins present in the membrane fractions.

15. The prior art rejections of the pending claims by **Husson et al** (1993), **Calenoff** (US Pat.5,567,594, filing date: December 20, 1993) , **Bolin et al** (1995), **Doig et al** (1994), **Alemohammad** (US Pat.5,262,156), **Pronovost et al** (US Pat. 5,814,455 and 5,846,751) , and **Ruiz et al** (WO94') are traversed as a group through asserting that:

a.the fractionation of the Helicobacter protein preparations of the prior art was on gels and the bands have similar sizes to the proteins now claimed, but are not the claimed invention;

b.the phrase "consisting essentially of" is recited in all of the claims, and the basic characteristic is the "54, 50, 32-35, or 30 kDa Helicobacter proteins that are in highly purified form."

16. It is the position of the examiner that:

a. Husson et al utilized a series of ultracentrifugations, which selected for and separated out an outer membrane protein preparation (see page 2695, col. 1, paragraph 3, col. 2, paragraph 2). The individual outer membrane proteins were visualized on SDS-PAGE, which showed a very specific number of bands which did not blur the gel;

b.Calenoff conducted a series of solvent fractionations (see Table 1, col. 6) and column fractionations (see all figures) over a range of more that 20 tubes, which were evaluated based upon the presence of immunoreactivity for specific Helicobacter proteins. The resulting Helicobacter proteins were highly purified, and specific epitopes (peptides and polypeptides identified based upon antibody immunoreactivity, (see Calenoff, col. 7, lines 56-67, col. 8,lines 1-40 and all claims), monospecific antibodies (see Calenoff, col. 20), and methods of detecting the presence of H.pylori allergens and antibodies in a sample , as well as vaccines with carriers, adjuvants and pharmaceutically acceptable diluents and additives (see col. 19, lines 14-53);

c. Bolin et al was applied against claims 10-11 which are directed to monospecific antibody compositions, and methods of detecting an antibody or antigen in a biological sample. Outer Helicobacter membranes were produced through a series of steps which included sonication, low and ultra speed centrifugation, and electrophoresis.

d. Doig et al also prepared compositions of outer membrane proteins of Helicobacter pylori through fracturing membranes with a French press, treatment with specific enzymes to remove RNA and DNA, along with a series of centrifugations to isolate the desired proteins. The proteins were combined with Milli Q water (pure water) (see Doig et al, page 4527, col. 2, page 4528, Table 1).

e.Alemohammad (US Pat.5,262,156) produced enriched compositions of Helicobacter pylori antigens (claims), as well as affinity purified (monospecific antibodies) to Helicobacter

antigens (see col. 7, lines 34-55). The Helicobacter pylori antigen composition was shown to evidence specificity for H.pylori (see Figure 2, col. 7, lines 31-32).

f. Pronovost et al (US Pat. 5,814,455 and 5,846,751) also utilized a series of column fractionations to achieve the desired isolated Helicobacter antigens (see col. 5, lines 1-21); and

g. Ruiz et al (WO94') at page 4, lines 36-37 and page 5, lines 1-2, teach the utilization of recombinant segments of Helicobacter pylori urease protein, polypeptide fragments, wherein the recombinant compositions would be free of other H.pylori proteins. The H.pylori protein and polypeptide compositions were produced with the production/induction of antibodies for therapeutic and diagnostic purposes (see page 6, lines 22-33).

All of the Applied references traversed as a group disclosed means and methods that included far more than just running a composition on an SDS-PAGE gel, in order to obtain the desired Helicobacter pylori outer membrane protein(s). The references applied to the claims are maintained for reasons of record, especially paper number 15.

17. Applicant asserts that the claimed proteins/polypeptides and peptides are in "highly purified form".

18. It is the position of the examiner that none of the claims recite any specific level of purity and the instant specification defines the phrase "substantially purified form" to be "understood to mean that the protein is separated from the medium which it exists naturally"; this would include a whole cell lysate composition, which is not a highly purified form of a single protein.

Applicant's arguments are not commensurate in scope with the instantly claimed invention.

19. While Applicant's Representative defines one of the basic characteristics of the claimed invention, the basic and novel characteristic of the instantly claimed inventions was not pointed out in the narrative on page 5, of the Amendment submitted August 25, 2003. No distinguishing characteristics, starting material or combination of reagents have been set forth in claims 1-3, 5-7, 10-11, 14-20, 22-24, 28-29, 33-41 that define over the prior art of record.

20. The rejection of claims 19-20 and 41 under 35 U.S.C. 102(b) as anticipated by Ferrero et al (1995) is traversed on the grounds that : "claim has been amended to specify a composition that **consists** of certain antigens, none of which is 54 kDa; claim 19 is now drawn to a composition that **consists** of certain antigens, none of which is 54 kDA, and an additional Helicobacter polypeptide antigen; claim 20 is now drawn to a composition that consists of certain antigens, none of which is 54 kDa and a urease antigen; and claim 30 has been canceled without prejudice."

21. It is the position of the examiner that none of the pending claims recite closed language "consists of" as argued by Applicant. All of the claims recite "consisting essentially of" or open language (immunoreactivity with an antisera (claim 7, and compositions that depend therefrom). Applicant's arguments are not commensurate in scope with the instantly claimed invention. Additionally, despite the fact that many of the claims no longer recite the term "54

kDa", the claims still recite the phrase "of the order of 50" kDa, which includes an Helicobacter pylori antigen of about 54 kDa. The phrase "on the order of 50 kDa" is being read to permit variation in the relative molecular weight of the claimed proteins. The disclosure of Ferrero et al (1995) still anticipates the instantly claimed invention.

disclose Helicobacter urease holoenzyme (contains UreA subunit of 30 kDa and UreB: Helicobacter urease) together with a additional antigen identified to be a 54 kDa heat shock protein (see page 6499, col. 1, last sentence bridging to col. 2, first four lines). Recombinantly produced HspB (54 kDa) was combined with cholera toxin (adjuvant in 0.1M sodium bicarbonate) as an immunizing composition (see Table 2, narrative below Table, on page 6501 and page 6500, col. 1, paragraph 3). Two methods of detecting serum antibodies to the 54 kDa Helicobacter protein are disclosed, wherein the methods were immunoblotting and enzyme linked immunosorbent assay. The biological sample was contacted with the polypeptide and the immune complex formed between the serum antibodies and the polypeptide detected (see page 6500, col. 1, paragraphs 2; Figure 2, page 6501 and col. 2, paragraph 1, page 6501). Ferrero et al anticipate the newly amended or newly submitted claims 1, 19-20 and 29-30.

***New Claims/New Claim Limitations/New Claim Amendments/New Grounds of Rejection***

***Claim Objections***

22. Claim 17 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel

the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. The scope of claim 17 not only recites the claim limitations of claim 1, from which it depends, but also recites additional species which are fragments of the proteins of claim 1, thus broadening the scope of claim 1.

***Claim Rejections - 35 U.S.C. § 112***

23. Claim 7 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 7 recites the phrases "derived from the protein by fragmentation" and "recognized by an antiserum raised by the protein". These phrases define process steps, but , what the process step produce is unclear. The product resulting from chemical enzyme fragmentation with any proteinase, or fragmentation through a molecular sieve, does not defined by any specific chemical structure, or biological function. The resulting protein must evidence immunological reactivity, but the binding specificity of the antibody is not defined to be any specific epitope or epitopes, is not defined by a deposited monoclonal antibody which would predictably, and reproducibly immunoreact with the same protein or fragment of a protein, and what the identifying characteristics of the claimed protein or fragment with respect to overall relative molecular weight, structure and biological function is unclear. The antibody must only recognize a Helicobacter protein or polypeptide, the specificity may be non-specific

recognition, or specific recognition, through the broad recitation of the phrase "recognized by". The invention is not distinctly claimed based upon an antiserum, the nature only being only defined by the phrase "raised against the protein of the composition of claim 1", when claim 1 only defines the source of the protein to be Helicobacter pylori of the recited molecular weight; the relative molecular weights each defining a genus of proteins of a specific size, but no single specific protein (ie any enzyme). In light of the fact that Helicobacter pylori produces about 1,590 proteins (Tomb et al, 1997), the Applied Prior art references (all of record) providing evidence that a plurality of proteins of a common relative molecular weight are known to be produced by Helicobacter pylori, and that at least about 28 different species (Helicobacter species acinoyx; bilis; bizzozero; canis; chlorum; cholecystus; cinadei; coli; colifelis; felis; fenelliae; heilimannii; hepaticu; jejuni; mainz; mesocricetus; muetelae; muridarium; mustalae; nemestrinae; oedipus; pametensis; rappini; rodentium; salmonii; salomonis; suncus; trogontum; upsaliensis) of Helcobacter are known. What the claimed Helicobacter proteins and polypeptides are, that are present in any other species that would be recognized by the antiserum is unclear because the antiserum, and what the fractionation process produces are unclear.(polyclonal antiserum produced in different animals or even the same animal will not produce the same cocktail of antibodies (see page 3, section 1.2.1, Ailsa M. Campbell, 1991, reference provided herewith).

Claim 7 recites the phrase "in substantially purified form" and refers back to either the polypeptide or the protein. Which species recited in the claim is present in purified form? The

Helicobacter protein appears not to be purified; only the polypeptide derived from the protein is in a substantially purified form. The invention is not distinctly claimed if both species recited in the claim are not purified.

***Claim Rejections - 35 U.S.C. § 101***

24. 35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

25. Claim 7 is directed to a Helicobacter protein that is not isolated and purified;the claimed invention is directed to non-statutory subject matter .

***Claim Rejections - 35 USC § 112***

26. Claims 7,11, 14-15 and 17 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 7,11, 14-15 and 17 depend directly or indirectly from claim 1 and are directed to Helicobacter proteins and polypeptide fragments that are recognized by an antiserum produced to the Helicobacter pylori protein(s) in the composition of claim 1, and to monospecific antibodies that recognize the protein or polypeptide that is recognized by the antiserum raised to by the protein of claim 1, used in methods of detecting. The compositions of claim 1 are not defined as specific products produced by any specific process, but may be any Helicobacter pylori membrane protein of the recited relative molecular weights. The proteins and polypeptides of claim 7 are Helicobacter proteins, but are not limited to being obtained from Helicobacter pylori, but need only to be recognized by an antiserum raised to any one of the proteins of claim 1.

Currently, at least 28 different Helicobacter species have been isolated, in addition to Helicobacter pylori. The instant specification has only described Helicobacter pylori proteins, and two specific N-terminal polypeptides (SEQ ID NO 1, and 2), and not the genus defined by an antiserum that evidences immunocross-reactivity with proteins present in one or more species of Helicobacter, the antibodies not being required to recognize any specific sequence or region of the claimed proteins or polypeptides.

In light of the fact that Helicobacter pylori produces about 1,590 proteins (Tomb et al, 1997), that the Applied Prior art references (all of record) provide evidence that a plurality of proteins of a common relative molecular weight are known to be produced by Helicobacter pylori, and that at least about 28 different species (Helicobacter species acinoyx; bilis; bizzozero; canis; chlorum; cholecystus; cinadei; coli; colifelis; felis; fenelliae; heilimannii; hepaticu; jejuni; mainz; mesocricetus; muetelae; muridarium; mustalae; nemestrinae; oedipus; pametensis; rappini; rodentium; salmonii; salomonis; suncus; trogontum; upsaliensis) of Helcobacter are known, the instantly claimed genus of proteins or polypeptides from any Helicobacter source that need only be recognized by an antiserum raised to any one of the members of the claimed genus of proteins of the recited molecular weight of claim 1, has not been described in such a way that one of skill in the art at the time of filing had possession of the claimed invention.

What the claimed Helicobacter proteins and polypeptides are, that are present in any other species that would be recognized by the antiserum (polyclonal antiserum produced in different animals or even the same animal will not produce the same cocktail of antibodies has not been described because what chemical structures the antiserum recognizes (epitopes, conformational epitopes, linear epitopes, a plurality of recross reactive antigenic sites) has not been described.

While enzymatic treatment of proteins is possible, the instant specification does not show the production of the claimed genus of fragments now claimed. Evidence was made of

record to show that a plurality of Helicobacter proteins evidence the recited relative molecular weights of 54, 50, 32-35 and 30 kDa. The 50 kDa protein evidencing the N-terminal amino acid sequence SEQ ID No. 1, is only a single species of fragment recited in the claims. Additional proteins or polypeptide fragments that comprise any other structure have not been claimed, nor described in the instant specification based upon the fact that the protein containing compositions have not been described by structure correlated with biological function.

The claimed fragments of whole proteins have not been described by structure correlated with function, other than a single claimed species (SEQ Id NO 1). SEQ ID NO 1 does not provide written descriptive support of a representative number of species to enable the instantly claimed genus of polypeptide fragments.

What has not been described, has not been enabled. One can not enable, what one has not described. In light of the fact that the genus of fragment polypeptides has not been described, monospecific antibodies to any fragments other than SEQ ID NO 1, have not been described. Monoclonal antibodies are monospecific antibodies directed to single epitopes. A representative number of epitopes have been disclosed or described in the instant specification for the now claimed genus of monospecific antibodies (claims 10-11, method of using claim 14) other than the sequence recited in claim 4, provided by SEQ ID NO 1. The genus of claimed monospecific antibodies has not been described, nor has the genus of fragment polypeptides been described to which antibodies bind. Utilization of monospecific antibodies (monoclonal antibodies or monospecific antibodies to fragments not described, or fragment polypeptides) or C-terminal fragment polypeptides not described, which are to be used in a method of detecting Helicobacter antigen or Helicobacter antibodies, respectively, in a biological sample have not been described in light of the genus of fragment polypeptides, or mutant fragment polypeptides (definition provided in instant specification) have not been

described in such a way that one of skill in the art would have recognized that Applicant had possession of the genus at the time of filing.

27. Claims 7,11, 14-15 and 17 under 35 U.S.C. 112, first paragraph (enablement), as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims are directed to polypeptide fragments of proteins (claims 7, and 17), a method of utilizing the polypeptide fragments, monospecific antibodies immunoreactive thereto (claim 11). The amino acid sequences contained in the claimed genus of about 54 or 50, or, 32-35 or 30kDa proteins has not been disclosed or described, other than SEQ ID NO 1 or 2. The claimed fragment polypeptides are not of any specific size and do not evidence any specific biological function. The claimed fragment polypeptides are not required to evidence any conserved essential structure, function or size or combination of these characteristics to insure the polypeptides would or could serve as an immunogen or diagnostic antigen, nor are they required to be made by any specific process. "Limited enzymatic digestion" would or could change the protein molecule, but where these changes can be made to preserve immunoreactivity has not been described. Lin et al (1988, abstract) teaches that limited enzymatic digestion of a bacterial protein resulted in polypeptide fragments that did not react with monospecific antibodies, which reacted with the intact protein (see entire abstract). Even limited enzymatic digestion can alter immunoreactivity based upon where and how many cleavage points are introduced in to the protein. No guidance and teaching has been provided to insure immunoreactivity of the fragment polypeptides with diagnostic antibodies associated with disease; Hpylori being a human pathogen. A genus of fragment polypeptides have not been described; essential conserved portions (fragment polypeptides) have not been taught in such a way that the person of skill in the art would know that the fragment polypeptide's protective or diagnostic value have been preserved.

The person of skill in the art would de novo be required to identify and determine which of the many possible fragment polypeptides encompassed by the definition of polypeptides of the instant specification would serve for the asserted purposes of being a diagnostic or vaccine antigen, in light of the fact that no specific guidance or teaching as to what portions of the whole protein are essential for maintaining the desired biological and chemical characteristics, nor has any specific guidance been provided as to where changes could be made to predictably result in a polypeptide with the asserted and critical characteristics represented by the whole protein; the claimed invention is not enabled for the claimed genus of polypeptide fragments recognized by any antiserum raised to a Helicobacter pylori protein, wherein the polypeptide fragments are not required to be from Helicobacter pylori, nor is it enabled for monospecific antibodies to the fragment polypeptides, and the utilization of the polypeptide fragments and monospecific antibodies in a method of detecting the presence of any Helicobacter in a biological sample.

***Claim Rejections - 35 U.S.C. § 102***

28. Claims 1,3,7,19, 22, 28, 33, 35, and 41 are rejected under 35 U.S.C. 102(b) as being anticipated by Exner et al (July 1995).

Exner et al disclose the instantly claimed invention directed to isolated Helicobacter pylori membrane fraction proteins of about 50 kDa. Exner et al disclose three proteins of about 50 kDa, specifically 48, 49 and 50 kDa and are outer membrane proteins of Helicobacter pylori (see title, abstract). The proteins were isolated and purified and resuspended in a 10mM tris-HCL buffer of pH 8.0, a form that is acceptable to humans (see page 1567, col. 2, paragraph 1, last few lines of first paragraph). The reference anticipates the instantly claimed invention. .

29. Claims 1, 5, 7, 10-11,17-20,24, 28, 33-37,41 are rejected under 35 U.S.C. 102(e) as being anticipated by Michetti et al (US Pat. 5,972,336; filing date July 1993).

Michetti et al disclose the Helicobacter pylori compositions that comprise urease (see col. 5, lines 54-8), proteins/polypeptides/peptides (see col. 3, lines 29-31), a protein the order of 30 kDa protein (see col. 5, line 55 (28 kDa), together with an additional Helicobacter antigen (urease, 63 kDa), an adjuvant ( see col. 5, lines 2-4 ) and a pharmaceutically acceptable carrier (see Michetti et al, col. 4, lines 59-67). The reference also discloses a monospecific antibody immunoreactive to the Helicobacter pylori antigen (see col. 4, lines 10-14). The reference anticipates the instantly claimed invention (see claims 21-22, 25-26).

30. Claims 1, 5, 7, 10-11,17-20,24, 28-29, 33-37,38-41 are rejected under 35 U.S.C. 102(e) as being anticipated by Labigne et al (US Pat. 6,248,330; effective filing date May 1995).

Labigne et al disclose the Helicobacter pylori compositions that comprise urease (see col. 3, lines 38-40), proteins/polypeptides/peptides (see claims), a protein the order of 30 kDa protein, together with an additional Helicobacter antigen (urease, 66 kDa) and/or a heat shock protein on the order of 54 kDa (58 kDa, see col. 4, lines 30-37), an adjuvant ( see col. 9, lines 4-15) and a pharmaceutically acceptable carrier (see claims 11-12 and 14). The reference also discloses a monospecific antibody immunoreactive to the Helicobacter pylori antigen (see 10, lines 40-64). The reference anticipates the instantly claimed invention (see all claims).

31. Claim 10-11 and 17 are rejected under 35 U.S.C. 102(b) as being anticipated by Vijgenboom et al (1994) as evidenced by a sequence alignment of SEQ ID NO 1.

Vijgenboom et al (1994) disclose a composition of antibodies that is highly cross reactive with a polypeptide fragment that comprises a highly conserved amino acid sequence across a plurality of bacteria (see page 990, col. 1, line 5; Table 2; page 993, Fig 6 and 7). The antibodies of Vijgenboom et al (1994) inherently anticipate the instantly claimed invention in light of the evidence that the immunogenic polypeptide of H.pylori shares 18 identical amino acids over a region of 21 Helicobacter pylori amino acids (SEQ ID NO 1) and the Ecoli amino acid sequence

for Ef-tu share 90.5 % sequence identity over 19 amino acids at the N-terminal of the Helicobacter pylori SEQ ID NO 1 (see alignment provided.), and the antibodies that bound the immunogenic polypeptide of Vijgenboom et al also specifically bound to the corresponding E.coli polypeptide as well.

32. Claim 7, 10-11 and 17 are rejected under 35 U.S.C. 102(b) as being anticipated by Kamla, V et al (1992) as evidenced by a sequence comparison with SEQ ID NO 1.
(Claims 10-11) Kamla, V et al (1992) disclose a composition of monospecific antibodies that is highly cross reactive with a polypeptide fragment that comprises a highly conserved amino acid sequence across a plurality of bacteria (see Table 1, page 76; Mabs CA6 and GB8 reacted with antigen from non-mollicutes, and KD2, ME3 and RB3 reacted also with Acholeplasma (see page 77, col. 1, paragraph 1, middle of paragraph). The antibodies of Kamla, V et al (1992) inherently anticipate the instantly claimed invention in light of the evidence that the immunogenic polypeptide of H.pylori shares N-terminal identical amino acids over a region of Helicobacter pylori amino acids (SEQ ID NO 1) and the Ecoli amino acid sequence for Ef-tu share 90.5 % sequence identity over 19 amino acids at the N-terminal of the Helicobacter pylori SEQ ID NO 1 (see alignment provided.) and the antibodies that bound the immunogenic polypeptide of Kamla, V et al also specifically bound to the corresponding E.coli polypeptide as well.
(Claims 7, and 17) Additionally, Kamla, V et al disclose an isolated immunogenic polypeptide fragment of the protein of claim 1, wherein the polypeptide fragment comprises a portion of a highly conserved amino acid sequence of SEQ ID NO 1, see (Table 1, N-terminal amino acid sequences that comprise a polypeptide fragment of the protein of claim 1). The polypeptide of Kamla et al, was derived by (process limitations) fragmentation (N-terminal amino acid sequence fragmentation) and was in purified form, and would be recognized by an antiserum raised to the protein of claim 1. In light of the claimed polypeptide need only evidence

characteristics derived from a Helicobacter polypeptide, defined by immunoreactivity with an antiserum, the polypeptides of Kamla et al inherently anticipate the instantly claimed invention, in light of the fact that the polypeptides of Kamla et al comprise a common amino acid sequence that is highly conserved and antibody cross reactive.

Inherently the reference anticipates the now claimed invention. Atlas Powder Co. V IRECA, 51 USPQ2d 1943, (FED Cir. 1999) states "Artisans of ordinary skill may not recognize the inherent characteristics or functioning of the prior art...However, the discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer. "The Court further held that "this same reasoning holds true when it is not a property but an ingredient which is inherently contained in the prior art".

***Conclusion***

33. This is a non-final action.

34. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Tiboni, O et al (1989) is cited to show immunochemical cross reactivity of EF-tu between various bacteria with a polyclonal antibody.

35. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ginny Portner whose telephone number is (703)308-7543. The examiner can normally be reached on Monday through Friday from 7:30 AM to 5:00 PM except for the first Friday of each two week period.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached on (703) 308-3909. The fax phone number for this group is (703) 872-9306.

The Group and/or Art Unit location of your application in the PTO will be Group Art Unit 1645. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to this Art Unit. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Vgp

November 5, 2003

MARK NAVARRO
PRIMARY EXAMINER